

REMARKS

Claims 1-116 were previously cancelled. Claims 126, 133, 138, 139, 142, 143 and 149-178 have been withdrawn. Applicants reserve the right to file divisional applications directed to the withdrawn subject matter. Claim 117 has been amended to further define the current invention. Support for the amendment may be found throughout the specification, specifically at page 14, lines 15-19 and page 17, lines 2-28. Claim 148 has been amended to correct a minor informality. No new matter has been added. Claims 117-125, 127-132, 134-137, 140, 141, 144-148, 179 and 180 are currently pending.

Claim Objection

Claim 148 is objected to for minor informalities. Claim 148 has been amended. Withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 117-125, 127-132, 134-137, 140, 141, 144-148, 179 and 180 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the phrase "wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide duplex when the displacer is introduced into the recipient polynucleotide duplex" adds new matter to the claims. The Examiner states that the claim could be read to read that the displacer changes at least one nucleotide in the recipient polynucleotide duplex of a triplex displacer-recipient complex. (See Office Action page 3).

Applicants respectfully traverse the rejection. The specification contains a detailed discussion of single stranded displacers which are not hybridized to a linker strand and that are capable of initiating triplex formation. (See Specification at page 16, line 30). The single-stranded displacer strand contains at least one modified nucleotide. (See Specification page 17, line 27 to page 18, line 16). As with the recipient polynucleotide duplex, the change to the nucleotide in the polynucleotide duplex of a triplex displacer-recipient complex will occur when the new strand is introduced.

In addition, Applicants respectfully submit that the labeling of the displacer-recipient complex is irrelevant to the subject matter of claim 117. The displacer recipient complex of

the present invention comprises several sections, each with a varying number of nucleic acid strands. The central portion of the complex comprises the initial portion of the overhang of the displacer strand which is complementary to and binds to the double-stranded recipient molecule. This results in a triple-stranded central portion. The downstream portion of the displacer recipient comprises the displacer-linker duplex which is double stranded. The upstream portion of the displacer recipient molecule comprises the displaced nucleic acid which is single stranded. Thus, the phrase "displacer recipient complex" can not be defined in terms of a duplex or triplex. Rather, it is a descriptive term encompassing the molecule that exists after hybridization of the displacer linker composition to the recipient duplex. A person of skill in the art would have the ability to visualize the resulting molecule in the absence of any label. Thus, claim 17 satisfies the written description requirement. Withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 117-125, 127-132, 134-137, 140, 141, 144-148, 179 and 180 are rejected under 35 U.S.C. §112, second paragraph as failing to comply with the written description requirement. The Examiner states that claim 117 is vague and indefinite because it is unclear as to if the displacer recipient complex is a duplex or a triplex.

Applicants respectfully traverse the rejection. As explained in detail above, the phrase "displacer recipient complex" can not be defined in terms of a duplex or triplex. Rather, it is a descriptive term encompassing the molecule that exists after hybridization of the displacer linker composition to the recipient duplex. A person of skill in the art would have the ability to visualize the resulting molecule in the absence of any label. The labeling of the displacer-recipient complex as either a duplex or triplex is not relevant to the subject matter of independent claim 117. Withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §102(e)

Claims 117-119, 121, 125, 134-136, 144, 145, 179 and 180 are rejected under 35 U.S.C. §102(e) as being anticipated by Lin et al. (U.S. Patent No. 5,214, 136; hereinafter "Lin"). The Examiner cites three main reasons: (1) "the nucleic acid displacer taught by Lin *et al.* has the ability to changes at least one nucleotide or a nucleotide sequence in the recipient polynucleotide duplex which is available in nature when the displacer is introduced

into the recipient polynucleotide duplex”; (2) “when the displacer is introduced into the recipient polynucleotide, the recipient polynucleotide recited in claim 117 is not part of a nucleic acid displacer composition”; and (3) “the phrase ‘wherein said displacer changes at least one nucleotide or a nucleotide sequence in said recipient polynucleotide when the displacer is introduced into the recipient polynucleotide nucleotide’ recited in claim 117 is not a structural limitation of the claim, but is a functional limitation of the claim.” (See Office Action page 5-7). The Examiner further contends that the claims do not require that the displacer is introduced to the recipient polynucleotide and then displaces an original strand of the recipient polynucleotide, as previously argued by Applicants. The Examiner also states that the displacer taught by Lin has the ability to change at least one nucleotide in the recipient polynucleotide complex upon introduction of the displacer, thus Lin does teach that the displacer changes at least one nucleotide in the duplex. Finally, the Examiner states that the claims do not require that the oligo or polynucleotide displacer can inhibit the activity of the target RNA or DNA. (See Office Action page 8-9).

Applicants respectfully traverse the rejection. A rejection under Section 102, an Examiner must show that each and every element recited in the claimed invention is taught by a single reference. (See MPEP §2131).

Lin teaches oligonucleotides derivatized to at least one anthraquinone at a position other than the 5' terminus. These compounds enhance hybridization to target DNA or RNA without the loss of specificity while providing enhanced stability to nucleases. The Examiner points to Table 4 in his analysis of the Lin patent. A close reading of the portion of Example 5 -- “Specificity of Hybridization” (data summarized in Table 4) describes conventional hybridization of the modified oligomers to RNA. Thus, the modified oligomers were hybridized to *single-stranded* RNA complexes. (See Col. 9, lines 9-12). A duplex is formed only after binding of the modified oligomers.

In contrast, the present invention requires binding of the displacer composition to a recipient polynucleotide *duplex*. The displacer complex is complementary to and base pairs with one strand of the recipient polynucleotide duplex. Claim 117 clearly recites the structural limitation of a recipient polynucleotide duplex. Lin, therefore, does not recite each and every limitation of claim 117 and is therefore does not anticipate the currently claimed invention. Withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §103(a)

Lin *et al.* in view of Dattagupta *et al.*

Claims 146 and 147 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lin as applied above and further in view of Dattagupta *et al.* (U.S. Patent No. 4,737,454; hereinafter “Dattagupta”). The Examiner contends that there is motivation to combine the references because the simple replacement of a type of label on the displacer molecule would have been obvious because the labels are used for the same purpose. (See Office Action pages 10-11). The Examiner also states that the displacer taught by Lin has the ability to change at least one nucleotide in the recipient polynucleotide complex upon introduction of the displacer. The Examiner then concludes that Lin does teach that the displacer changes at least one nucleotide in the duplex. (See Office Action page 13).

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness. If the Examiner does not satisfy this burden, then the Applicant is not obligated to submit evidence of non-obviousness. (See M.P.E.P. §2142 at 2100-133 (8th ed., incorporating Revision No. 5, August 2006)). The recently revised Examiner guidelines for assessing obviousness set forth detailed requirements based on asserted rationales for obviousness. The Rationales To Support Rejections Under 35 U.S.C. §103 provide the following possible rationales:

- (A) Combining prior art elements according to known methods to yield predictable results;
- (B) Simple substitution of one known element for another to obtain predictable results;
- (C) Use of known technique to improve similar devices (methods, or products) in the same way;
- (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
- (E) “Obvious to try” – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
- (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

(See MPEP 8th Edition, rev. 6, §2141).

Applicants understand this rejection to conform to rationale G quoted above. The MPEP further sets forth the requirements for an obviousness rejection under this rationale:

To reject a claim based on [rationale G], Office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:

- (1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
- (2) a finding that there was reasonable expectation of success; and
- (3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

The rationale to support a conclusion that the claim would have been obvious is that “a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success.” *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006). **If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.**

(See MPEP 8th Edition, rev 6, §2143).

For at least the following reason, the Examiner has not shown that claims 146 and 147 are obvious over Lin.

As explained above, Lin does not teach a nucleic acid displacer composition which binds or complexes with a recipient polynucleotide duplex, as required by claim 117. Dattagupta does not cure the deficiencies of Lin. Like Lin, Dattagupta teaches only single stranded recipient molecules. Example 7, “Assay for the Label after DNA-DNA Hybridization” describes treating nucleic acids to form single-stranded products before

contacting with the labeled probe. (See col 12, lines 9-16). The references do not render the claims obvious because a person of ordinary skill in the art would have no motivation to combine the references, regardless of the type of label incorporated into the molecule. A person of skill in the art would have no reasonable expectation of success when combining the references because neither Lin nor Dattagupta teach a nucleic acid displacer composition which binds to or complexes with a recipient polynucleotide duplex. Claims 146 and 147 are not obvious over the combination of Lin and Dattagupta. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Lin et al.

Claim 148 is rejected under 35 U.S.C. §103(a) as being unpatentable over Lin as applied above. The Examiner states that there is motivation to alter the Lin displacer to form an artificially constructed polynucleotide comprising a naturally occurring recipient polynucleotide duplex hybridized to the nucleic acid displacer composition because Lin tested the oligonucleotide coupled to anthraquinone *in vitro* and *in vivo* and hybridized the molecule to a single stranded RNA molecule. (See Office Action pages 13-14). The Examiner then contends that Lin does teach changes in at least one nucleotide or nucleotide sequence in the recipient polynucleotide sequence.

Applicants respectfully traverse the rejection. As explained above, neither Lin nor Dattagupta teach a double stranded recipient polynucleotide duplex, a structural component required by claim 117 (from which claim 148 ultimately depends). A person of ordinary skill in the art would have no motivation to combine the references, regardless of whether the polynucleotide is naturally occurring or artificially constructed. Thus, there would be no reasonable expectation of success when combining the references because neither Lin nor Dattagupta teach a nucleic acid displacer composition which binds to or complexes with a recipient polynucleotide duplex. Claim 148 is not obvious over the combination of Lin and Dattagupta. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Oath or Declaration

The Office Action Summary sheet indicated that the oath or declaration is objected to by the Examiner. Applicants are directed to the "attached Office Action or form PTO-152" for further information. There is no explanation in the Office Action, nor is there an attached form PTO-152, as to the nature of the objection. Applicants respectfully request clarification of the objection to the oath or declaration.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,
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